Retrospective Study

Pathomechanism of Lower-level Discogenic Groin Pain and Clinical Outcomes of Percutaneous Endoscopic Discectomy for the Treatment of Discogenic Groin Pain

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Background: Groin pain can be induced by high-level (L1-L2 or L2-L3) lumbar disc herniation. However, 4.1% of patients with lower-level (L4-L5 or L5-S1) lumbar disc herniation also complained of groin pain. The pathomechanism of groin pain occurring due to lumbar disc herniation at and below the L4-5 levels is still unclear.

Objective: To investigate the afferent pathways of lower-level lumbar disc herniation induced groin pain. And evaluate the clinical results of transforaminal endoscopic discectomy treatment for discogenic groin pain.

Study Design: This retrospective observational study used an experimental design (institutional review board: HROH 201-C2-100).

Setting: The research took place in the Laboratory Research Center and spine center at The First Affiliated Hospital of Harbin Medical University.

Methods: Firstly, 14 adult Wistar rats were randomly divided into 2 groups: control group (the paravertebral sympathetic trunks were preserved) and experimental group (the paravertebral sympathetic trunks were resected). All Wistar rats were intraperitoneally anesthetized, and then 1 μL of fast blue was injected into the dorsal rami of L2 spinal nerves on the right side. Forty hours later, 2 μL of nuclear yellow was injected into the right posterior portion of the L5-L6 intervertebral disc. The L1 and L2 spinal ganglia were sectioned 8 hours later to observe fluorescently double-labeled cells and the effect of paravertebral sympathetic trunk resection. Secondly, 14 adult Wistar rats were anesthetized, and the right posterior portion of the L5-L6 intervertebral disc was electrostimulated to observe potential changes in the genitocrural nerve in the ipsilateral inguinal region. To evaluate the clinical outcomes of transforaminal endoscopic discectomy for the treatment of discogenic groin pain, between September 2015 and May 2017, transforaminal endoscopic discectomy was performed on 30 patients with lower-level discogenic groin pain. Outcomes were analyzed utilizing the visual analog scale, Oswestry disability index, and MacNab Criteria.

Results: The total proportion of cells in the right L1 and L2 spinal ganglia with fast blue/nuclear yellow double labeling was 3.33% and 3.41% (48 and 56), respectively. The number of fluorescently double-labeled cells in the resected paravertebral sympathetic trunk group was significantly less ($P < 0.01$). Electrical stimulation of the right posterior portion of the L5-L6 intervertebral disc could elicit action potentials in the ipsilateral genitofemoral nerve. All patients were followed for 12 months, and the visual analog scale score at 1 week, 1 month, 3 months, 6 months, and 12 months after the operation was 0.79 ± 0.55, 0.54 ± 0.55, 0.47 ± 0.65, 0.51 ± 0.65, and 0.69 ± 0.55, respectively, showing a significant decrease compared with the preoperative visual analog scale score ($P < 0.01$). Based on the MacNab scoring system, the effective rate was 100%, and the rate of good and excellent results was 93.3%.

Limitations: A relatively small number of patients and a short follow-up period.

Conclusions: Discogenic groin pain is transmitted by sympathetic nerves and appears in the area segmentally innervated by the anterior rami of the L1 and L2 spinal nerves. Posterolateral percutaneous transforaminal endoscopic discectomy and radiofrequency thermal annuloplasty are effective minimally invasive alternative treatments for discogenic groin pain.

Key Words: Discogenic groin pain, percutaneous transforaminal endoscopic discectomy, radiofrequency thermal annuloplasty

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Published studies suggest that high-level lumbar disc herniation (LDH) can cause groin pain (1). Based on our clinical experience, some patients with lower-level LDH also experience groin pain as their main symptom. However, nerve roots in the lower region of the lumber spine do not dominate the groin area, and it is often challenging for physicians to treat such patients (2). Since 2015, our department has treated 512 patients with disc herniation in the lower region of the spine (L4-L5, L5-S1). Of these patients, 59 had groin pain (11.5%): 19 (32%) complained mainly of groin pain and 40 (68%) had groin pain as well as lower extremity radiating pain. For patients with lower extremity radiating pain as well as groin pain, lumbar disc surgery successfully relieved the lower extremity radiating pain and significantly alleviated or completely eliminated the groin pain. The results suggest that there might be an anatomical connection between the lower lumbar disc and the anterior superior branches of the lumbar nerves (L1 and L2).

To investigate this hypothesis, we investigated the role of the paravertebral sympathetic trunks in the transmission of pain in animal and clinical studies. The main purposes of the studies were 1) to investigate the mechanism of discogenic groin pain and 2) to evaluate the diagnostic value and study the clinical outcomes of transforaminal endoscopic discectomy and bipolar radiofrequency annuloplasty for the treatment of discogenic groin pain.

Methods

Experimental subjects: A total of 28 adult Wistar rats (ordinary (I) class, male and female, weighing 250~300 g) were used in the studies. Fourteen were used for fluorescent retrograde double labeling, and the other 14 were used for electrophysiological detection. All animal studies were conducted in accordance with the ethics committee of Harbin Medical University requirements.

Neural pathway fluorescent retrograde double labeling: 14 rats were randomly divided into 2 groups. In the control group (sympathetic trunks preserved), after an intraperitoneal injection of 0.6% sodium pentobarbital, the skin was cut through the posterior midline, and the right dorsal muscle was revealed. The posterior branch of the L2 nerve was isolated in the right dorsal muscle. Under a microscope, 2 μL of 20 g/L fast blue was injected into the posterior branch using a microsyringe. The rats were re-anesthetized 40 hours later. Approximately 1.0 mm toward the right side of the posterior midline, 2 μL of 10 g/L nuclear yellow was injected into the right posterior wall of the L5-L6 disc with a microsyringe under direct vision. After 8 hours, the rats were still alive; we anesthetized them again, punctured the aorta from the left ventricle, and then perfused the body with 500 mL of solution containing 2% paraformaldehyde and 0.1% glutaraldehyde at 0.1 mol/L in phosphate buffer (pH 7.4, 4°C) for 1 hour. Immediately after perfusion, bilateral L1 and L2 spinal ganglia were obtained and fixed with the fixative solution for 3 hours. The spinal ganglia were then immersed in 0.1 mol/L phosphate buffer (pH 7.4, 4°C) containing 30% sucrose overnight. The spinal ganglia were sliced into sections 40 μm thick using a cryostat. Every other section was selected, for a total of 4 sections per specimen, and mounted on gelatin for observation with a fluorescence microscope using a UV filter (356 nm) (3). Labeled cells observed in the bright field mode were counted within 24 hours. In the experimental group (sympathetic trunks severed), following anesthesia, bilateral sections of the L1-L6 sympathetic trunks were severed intraperitoneally. The rest of the procedure was the same as that in the control group.

Electrophysiological detection: 14 Wistar rats were anesthetized. The right genitofemoral nerve was carefully separated using microsurgical techniques. We placed the stimulus electrode at L5-L6 and the guiding electrode in the right posterior side of the wall of the intervertebral disc to guide the unit discharge. The VC-9 double oscilloscope showed and recorded potential activity. The genitofemoral nerve was then severed, the exposed nerve tissue was immersed with liquid paraffin, and the area was closed. The rectal temperature of the rats in the control group was maintained from 36 – 38°C.

To exclude excitability of the genitofemoral nerve caused by current spreading, 2% procaine was used to block the genitofemoral nerve. First, the right posterior wall of the disc was electrically stimulated, and the unit discharge was recorded on the ipsilateral genitofemoral nerve. The genitofemoral nerve was then wrapped with 2% procaine; after 5 to 10 minutes, a negligible discharge was observed. The area was then irrigated with normal saline, and the discharge (n = 7) was observed after 30 minutes. The ipsilateral spinal ganglion (SG) was perfused with a low-calcium and high-magnesium solution to exclude chemical conduction. The electrical potentials recorded on the ipsilateral genitofemoral nerve were created by electrical stimulation of the right posterior wall of the disc, and the corresponding SG was then perfused with the low-calcium and high-magnesium solution (Ca^{2}+ 0.5 mmol/L, Mg^{2}+ 5 mmol/L). The change in the potential was recorded 30 minutes after perfusion (n = 7).

Clinical outcomes of percutaneous endoscopic dis-

cectomy and radiofrequency thermal annuloplasty for the treatment of discogenic groin pain: To verify the results of the animal experiments regarding the neural pathway of interest, we analyzed the results of clinical treatments. We selected patients with discogenic groin pain who were admitted to our hospital from September 2015 to May 2017. The inclusion criteria were as follows: 1) persistent groin pain, with or without lower limb pain, except for cases of organic hip and pelvis lesions; 2) lower LDH; 3) failure of pain medication, physical therapy, and other conservative treatments to effectively relieve the pain after 3 months of treatment; and 4) disc herniation-induced pain duplication with corresponding disc rupture shown by angiography (Fig. 1).

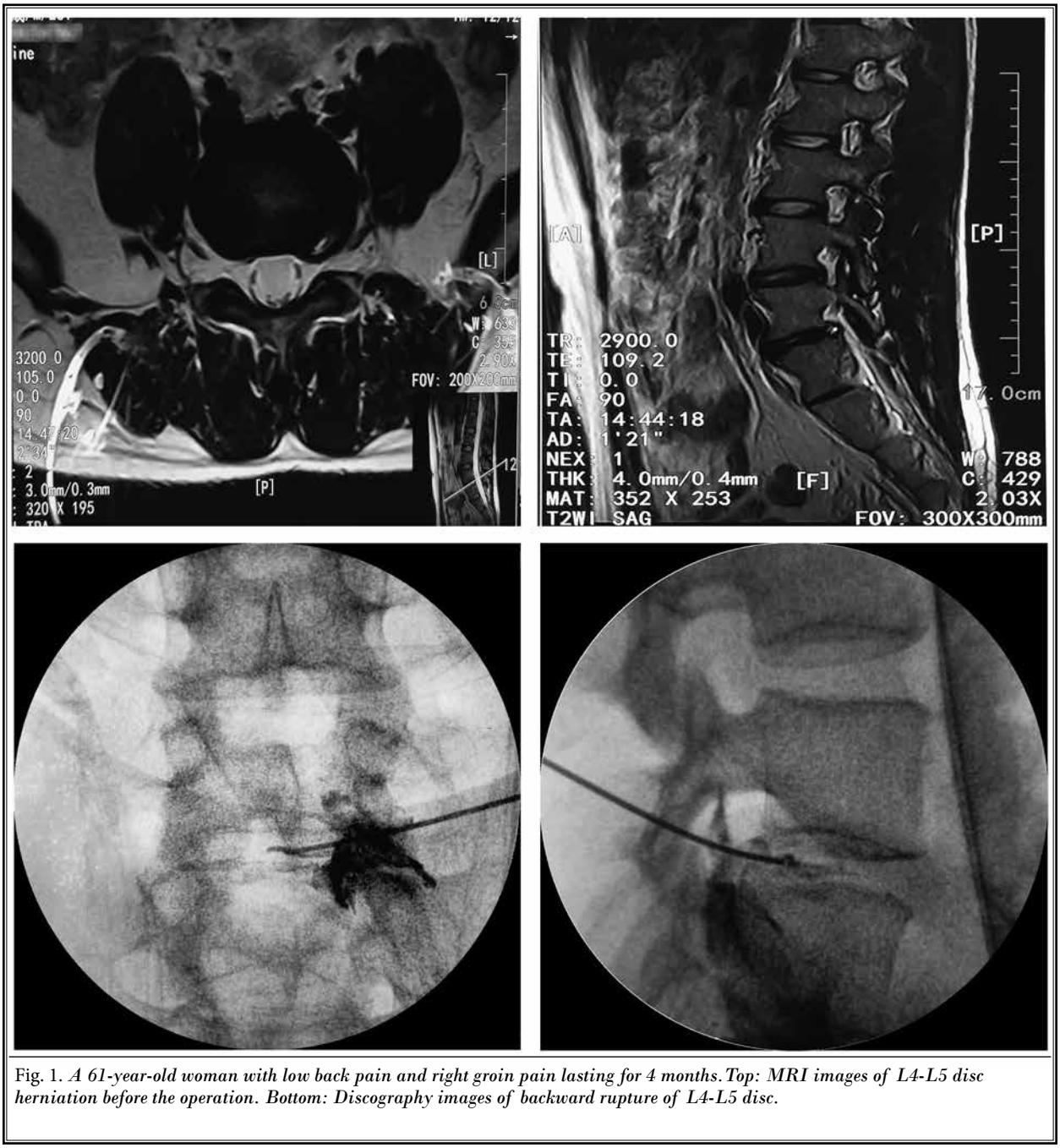

Fig. 1. *A 61-year-old woman with low back pain and right groin pain lasting for 4 months. Top: MRI images of L4-L5 disc herniation before the operation. Bottom: Discography images of backward rupture of L4-L5 disc.*

Thirty qualified patients were included in the study. There were 16 men and 14 women, with ages ranging from 45 to 72 years (52.31 ± 3.48 years) and pain durations ranging from one month to 10 years (2.36 ± 1.01 years). L4-L5 disc herniation was confirmed in 16 patients, L5-S1 disc herniation in 10 patients, and L4-L5 combined with L5-S1 disc herniation in 5 patients. Fourteen patients also had lower limb radiating pain. Preoperative low back pain VAS scores ranged from 5 to 8, with an average of 6.24.

Position and anesthesia: The patient assumed a prone position on the spine surgery bed, with both upper extremities away from the torso. A G-arm x-ray machine was used to produce standard lumbar lateral fluoroscopic images, which showed that the anteroposterior spinous process was located in the center of the pedicle and that the lateral vertebral endplates were parallel to each other. The surgical segment was located in the center of the fluoroscopic image. Anesthesia was induced with 0.5% lidocaine infiltration, assisted with midazolam conscious sedation.

Puncture: An 18-G spinal needle under video monitoring was inserted via a posterolateral approach to the dorsal 1/3 of the disc. The distance from the midpoint of the needle parallel to the endplate on lateral fluoroscopy was approximately 12 cm. The trajectory of the needle was set at an angle of 25° to 30° from the coronal view.

Pain-induced test and discography: For the discography diagnosis, the contrast medium was mixed with 9 mL of iohexol and 1 mL of sterilized methylene blue.

Instrument placement, endoscopic discectomy, and bipolar radiofrequency annuloplasty: A guide wire was introduced through the internal channel of the 18-G spinal needle, and the tip of the guide wire was inserted 1 – 2 cm into the disc; then, the needle was pulled out. The tapered tip of the soft tissue dilator was inserted along the guidewire until the head of the dilator reached the annulus. The dilator was tightly pressed against the annulus, the guidewire was removed, and the annulus fibrosus was anesthetized with 0.5% lidocaine via the center dilator tube. Full-length fenestration was used to open the window, and the working cannula was advanced along the dilator into the disc until the end of the working cannula was tightly pressed against the surface of the annulus fibrosus. The dilator was then removed, and the endoscope was inserted to observe the disc nucleus and annulus. Prominent degenerative nucleus pulposus was removed using the SPINENDOS endoscopic spine surgery system.

The Elliquence-triggered, flexible, bipolar radiofrequency electrode (Elliquence.LLC USA) was used under direct vision to ablate the granulation tissue and nerve endings that had grown into the fissure of the annulus fibrosus. Toward the end of the operation, bipolar radiofrequency was used for thermal coagulation and shrinkage shaping of the annulus fibrosus. At the end of the surgery, 4 mg of betamethasone was injected intraperitoneally to reduce the incidence of postoperative lower extremity sensory abnormalities.

Statistical Analysis

The SPSS software package for statistical analysis was used to analyze the data. Data are expressed as x ± s. The control and experimental groups were compared using the F test. Bilateral spinal ganglia in the control group were compared using the t-test. We used the visual analog scale (VAS) and MacNab scoring systems to evaluate the clinical outcomes. The VAS scores of lumbar pain preoperatively and at 1 week, 1 month, 3 months, 6 months, and 12 months after the surgery were statistically analyzed (F test). Statistical significance was defined as $P < 0.01$. MacNab scores were recorded at 12 months after surgery.

Results

Fluorescent Retrograde Double Labeling of Rat Lumbar Spinal Ganglia

In the right ganglia of the L1 and L2 segments, fast blue single-labeled neurons, nuclear yellow single-labeled neurons, and fast blue/nuclear yellow double-labeled neurons were observed. The fast blue-stained cells exhibited blue cytoplasm and a nonfluorescent nucleus. The nuclear yellow-stained cells exhibited nonfluorescent cytoplasm and a yellow nucleus. Fast blue/nuclear yellow double-labeled cells exhibited blue cytoplasm with a yellow nucleus. The number of fluorescently labeled cells in the L1 and L2 spinal ganglia of the rats in each group are shown in Table 1 and Fig. 2. There was no significant difference between the L1 and L2 spinal ganglia in the control group in the number of labeled cells ($P > 0.05$). However, both were significantly higher than that of the corresponding spinal ganglia in rats with severed sympathetic trunks. The difference between the 2 groups was significant ($P < 0.01$).

Electrophysiological Detection

Using the same stimulation parameters, electrical stimulation of the right posterior wall of the disc was performed, and potential changes in the ipsilateral

genitofemoral nerve were recorded. When the stimulation intensity was less than 32 V, no potential changes were observed; potential changes were observed at 32 V, and the potential gradually increased with increasing stimulation intensity (Fig. 3). When the stimulation intensity reached 40 V, the maximum value of the potential reached a peak. When the stimulation voltage was applied, there was an electrical change; when there was no stimulation voltage, no electrical change was observed. Changes in the direction of the stimulation

Table 1. *Fluorescently double-labeled cells in the L1 and L2 spinal ganglia of rats in each group (n = 7).*

Group	FB	NY	FB/NY	FB/NY%
Control group (L1)	891	562	48	3.33%
Control group (L2)	985	602	56	3.41%
Experimental group (L1)	103	79	3	1.64%
Experimental group (L2)	148	85	6	2.51%

*FB (fast blue single-labeled neurons); NY (nuclear yellow single-labeled neurons); FB/NY (fast blue/nuclear yellow double-labeled neurons); FB/NY% (FB/NY percentage)

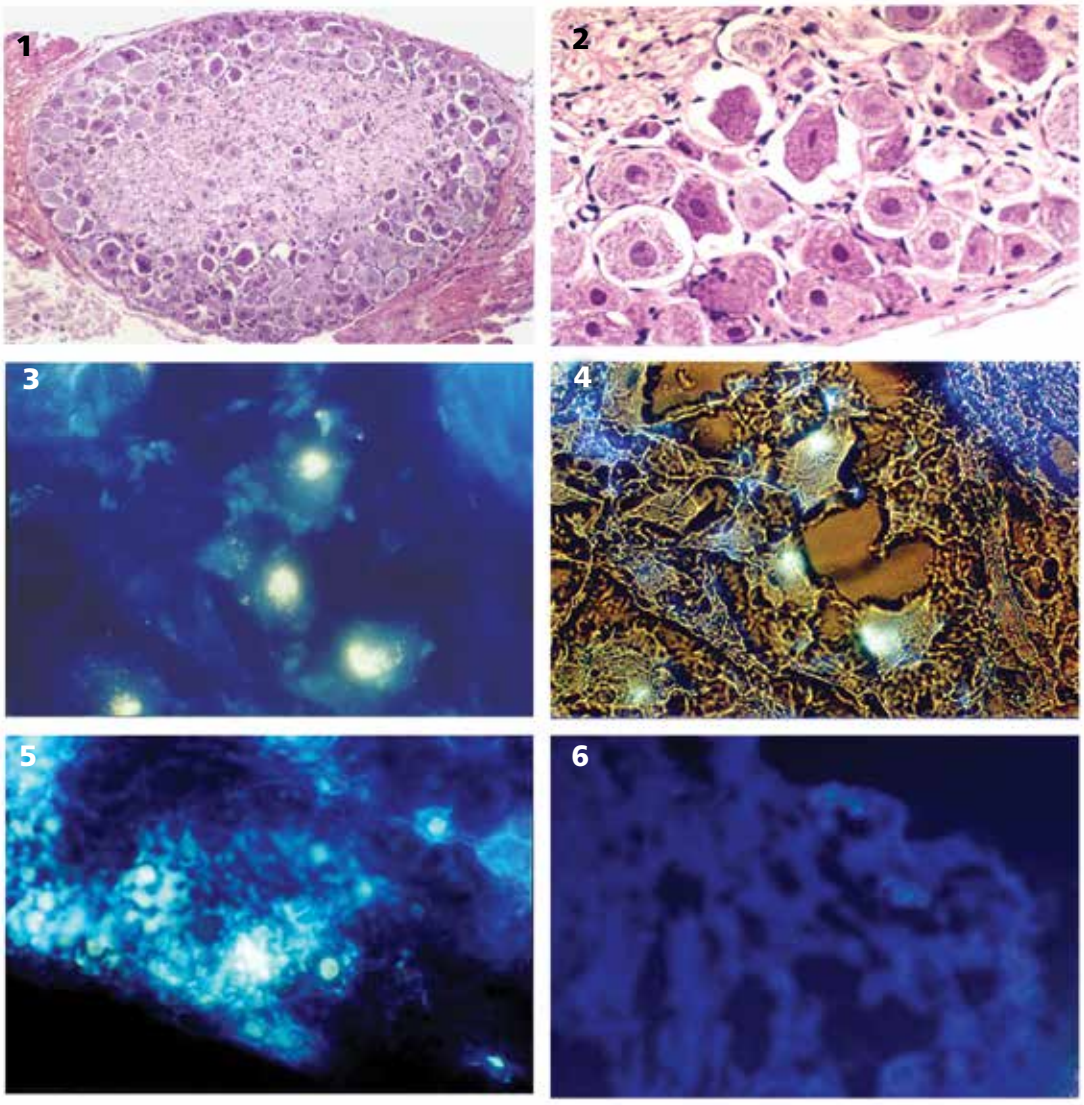

Fig. 2. *Fluorescent retrograde double labeling of rat lumbar spinal ganglia. 1. Normal rat lumbar ganglia (HE) × 200. 2. Normal rat lumbar ganglia (HE) × 400. 3. Double-labeled cells under a fluorescence microscope (x 400). 4. Double-labeled cells under a light microscope (x 400). 5. Double-labeled cells in the control group (x 200). 6. Double-labeled cells in the experimental group (x 200).*

current did not cause a change in the direction of the potential. Considering the characteristics of the action potential "absolute refractory period" and "relative refractory period," this potential can be determined as the action potential (Fig. 4). The action potential could be blocked by 2% procaine, and it reappeared after irrigation with normal saline. After perfusion with a low-calcium and high-magnesium solution, there was no significant difference between before and after perfusion in the latency or the maximum value ($P > 0.05$) (Fig. 5 and Table 2).

Results of Clinical Operations

All operations were successfully completed, and the patients were followed for 12 months. The VAS score of groin pain was 6.24 ± 0.97 before the operation, 0.80 ± 0.65 at one week after the operation, 0.56 ± 0.65 at one month after the operation, 0.48 ± 0.65 at 3 months after the operation, 0.52 ± 0.65 at 6 months after the operation, and 0.67 ± 0.58 at 12 months after the operation. Each postoperative score was significantly lower than the preoperative score ($P < 0.01$). No significant improvement after 6 months and 12 months was observed ($P > 0.05$). Based on the MacNab score at the 12-month follow-up visit, the results were excellent in 15 patients, good in 13 patients, and fair in 2 patients. The overall effective rate was 100%, and the overall rate of excellent and good results was 93.3%.

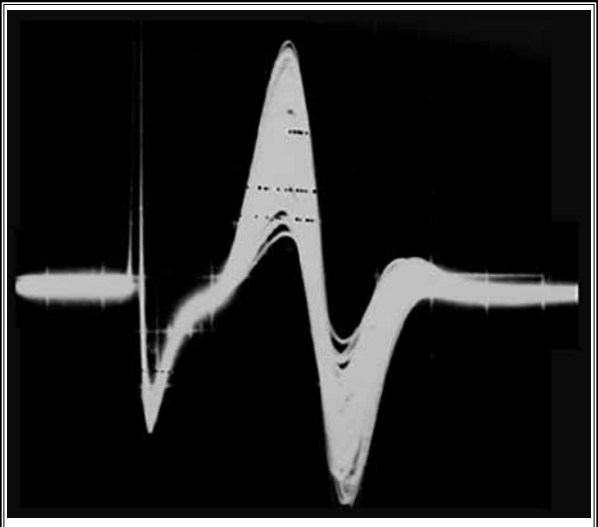

Fig. 3. *The peak of action potential increased with increasing stimulation intensity.*

Discussion

The theory that the posterior lumbar discs and the posterior longitudinal ligaments are controlled by the spinal nerves and sympathetic trunk (4,5) and that the sympathetic nerve can transmit pain (6) has been suggested in previously published studies. In 1997, Suseki et al (7) traced the origin of the small articular nerves of rats at L5-L6, suggesting that the small articular nerves of rats at L5-L6 originate from sensory fibers of the ipsilateral spinal ganglia and that paravertebral parasympathetic ganglia and facet joint spinal ganglia that reach L1 and/or L2 through the paraspinal sympathetic trunk could cause paravertebral sympathetic movement to transmit painful impulses from the lower lumbar facet joint to the inguinal region. The authors predicted that closure of the lumbar sympathetic trunk may partially resolve lower back pain. However, the relationship between lower posterior lumbar disc disease and inguinal pain remains unclear.

We used fluorescent retrograde double labeling and electrophysiological methods to trace the nerve conduction pathway between the lower lumbar intervertebral disc and the superior lumbar nerve. After fluorescein was injected into the right L2 lumbar nerve posterior branch and the right posterior wall of the

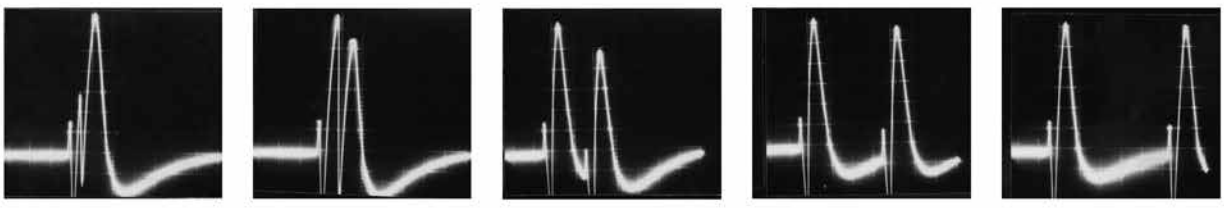

Fig. 4. *Action potential changes. The second stimulus fell during the absolute refractory period of the first action potential. The second stimulus fell during the relative refractory period of the first action potential, resulting in an action potential with a low peak. With extension of the relative refractory period, the peak value of the action potential gradually increased. The peak of the action potential was near normal. The second stimulus fell during the refractory period of the first action potential, and the 2 action potentials show the same peak.*

disc, double-labeled cells were found in the right L1 and L2 spinal ganglia. The results suggest that part of the nerve fibers distributed in the posterior annulus fibrosus and posterior longitudinal ligament of rats at L5-L6 could be derived from bilateral L1 and L2 spinal ganglia. Our results also suggest that lumbar parasagittal sympathectomy is an important neural pathway in disc-derived inguinal pain because when the sympathetic trunk was severed, the number of double-labeled cells was significantly reduced. However, pathways other than those involving sympathetic stem cells may also exist because double-labeled cells in the L1 and L2 spinal ganglia did not completely disappear.

In summary, some of the sympathetic nerve fibers originating from the bilateral L1 and L2 spinal ganglia distributed in the posterior annulus fibrosus and posterior longitudinal ligament at L5-L6 play a role in pain transmission. The results of our study are consistent with those of previous studies (4,7-13). It can be assumed that if the innervation pattern in humans follows a pattern similar to that observed in our study, then lower lumbar disc disease causes the stimulation and compression of the rear annulus fibrosus or posterior longitudinal ligament and the transmission of pain impulse by sympathetic nerve fibers in sympathetic ganglia to the L1 and L2 spinal ganglia, with some further transmission to the inguinal region along the anterior L1 and L2 branches. Then, the peripheral nerves release SP and other substances that caused symptoms. Therefore, we can speculate that disc-derived inguinal pain is mainly conducted by sympathetic nerves and involves the anterior L1 and L2 proprioceptor branches.

To further verify this neural pathway, we electrostimulated the right posterior wall of the intervertebral disc and changed the potential induced by the genitofemoral nerve in the ipsilateral inguinal region. The observed potential changes could be determined to be action potentials, although potential conduction may employ multiple pathways. To verify that the recorded change in the potential in the genitofemoral nerve reflected the potential transmitted by the corresponding sympathetic nerve segment, we severed the peripheral end of the genitofemoral nerve, wrapped it with procaine, and perfused the region with a low-calcium high-magnesium solution. The results show that there was no significant difference during the incubation period of the genitofemoral nerve relative to before perfusion ($P > 0.05$), and the amplitude of the action potential remained basically unchanged ($P > 0.05$). Excluding these possible routes of conduction, we determined that the stimulation of the right posterior wall of the ipsilateral disc was mediated by sympathetic nerves to reach the L1 and L2 ganglia, with the resulting reflections causing changes in the potential of the genitofemoral nerve.

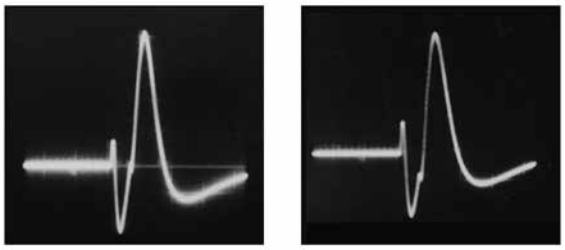

Fig. 5. *Changes in action potentials before and after perfusion of the low-calcium and high-magnesium solution.*
1. Before perfusion.
2. After perfusion.

Table 2. *Maximum action potential before and after perfusion with low-calcium and high-magnesium solution ($X \pm S$).*

	Samples	Latency (ms)	Maximum (mV)
Before	7	1.499 ± 0.024	30.714 ± 0.756
After	7	1.506 ± 0.017	30.714 ± 0.756
P		> 0.05	> 0.05

Based on the above animal studies, we further selected 30 patients with discogenic groin pain who underwent L4-L5 or L5-S1 transforaminal endoscopic discectomy and radiofrequency thermal annuloplasty to observe the clinical efficacy. Because the symptoms of discogenic groin area pain are atypical, it is challenging for both doctors and patients to choose appropriate treatment options. For patients with only symptoms of groin pain, it is difficult to decide whether to perform posterior lumbar interbody fusion surgery because of the potential surgical trauma and the lack of a guarantee that the groin pain will be eliminated. On the one hand, the surgeon may feel great pressure; on the other hand, the patient might hesitate to accept this treatment. To resolve this dilemma, we offered a minimally invasive treatment option. First, discography was used to diagnose and pinpoint the source of pain. If discography showed disc herniation and the pain in the groin area could be reproduced, then we performed transforaminal endoscopic discectomy and radiofrequency thermal annuloplasty to relieve the pain. Because of the many benefits of this minimally invasive approach, such as the minimal surgical trauma, it was easier for the patients to accept this type of treatment.

Our results show that discogenic pain in the groin area was reduced after the transforaminal endoscopic treatment, with postoperative VAS scores much lower than the preoperative scores. According to the MacNab scoring system, the overall effective rate of our treatment was 100% at 12 months after the operation, and the overall rate of good to excellent results was 93.3%. The results suggest that percutaneous endoscopic discectomy could be a safe and effective option for the treatment of discogenic groin pain.

Percutaneous endoscopic discectomy is performed through soft tissue expansion to establish surgical access and allow the endoscopic removal of degenerative nucleus pulposus. The procedure not only removes painful irritants but also creates a favorable environment for reducing the internal pressure of the disc and causing the annulus fibrosus to contract. Compared with traditional fusion surgery, percutaneous endoscopic discectomy is associated with minimal trauma. If performed appropriately, the surgical approach does not damage the important muscle function of the dorsal side and does not damage the biomechanical function of the spine; additionally, the function of sports segments can be retained. More importantly, even if the pain is not adequately relieved, this technique has no effect on other further surgical procedures (2).

Discogenic groin pain is strictly a manifestation of discogenic low back pain, and its pathogenesis is tearing of the inner annulus fibrosus and the cartilage endplates, causing the pain receptors in the outer layers of the annulus and the adjacent endplates to come into direct contact with proteoglycans in the nucleus pulposus. This contact induces a repair process in the annulus fibrosus, resulting in the growth of new blood vessels, nascent nerve endings, and granulation tissue into the annulus fibrosus (14). These nascent tissues are in constant contact with proteoglycans in the nucleus pulposus and stimulate sympathetic nerve fibers in the posterior annulus fibrosus and posterior longitudinal ligament to partially transmit pain signals (15,16) upward, triggering anterior branches of the L1 and L2 nerves and causing referred pain in the form of groin pain.

Tsou et al (17) performed a retrospective analysis of 113 patients with chronic lumbar discogenic pain who underwent percutaneous endoscopic discectomy. The patients were followed for at least 2 years, and the clinical outcomes were evaluated using a modified MacNab score. The results were satisfactory in 83 (73.5%) patients, including excellent results in 17 patients (15%), good in 32 (28.3%) patients, and fair in 34 patients (30.1%). The results were considered poor in 30 patients (26.5%), among whom 8 underwent lumbar fusion surgery, 7 underwent endoscopic surgery again, and 3 underwent lumbar laminectomy; 10 patients' pain improved after repeat surgery, and 12 patients did not undergo further surgery. Although the good rate in our study seems to be higher than previously reported findings, our study has a few limitations, including a relatively small number of patients and a short follow-up period. Further studies with larger samples and longer-term follow-up periods are needed.

Conclusion

In summary, discogenic groin pain is referred pain caused by low LDH and is transmitted by sympathetic nerves involving the anterior branches of the L1 and L2 nerves. Percutaneous endoscopic discectomy and radiofrequency thermal annuloplasty could be a safe and effective treatment option for discogenic groin pain.

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